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Examiner Julie Ha

CLAIMS

1. (Previously Presented) A method for the prophylaxis or therapy of at least one viral disease, comprising administering a physiologically effective dose of a pharmaceutical composition comprising at least one active substance that inhibits a cellular caspase such that a virus multiplication is inhibited.
2. (Previously Presented) The method of claim 1, wherein the caspase is caspase-3.
3. (Currently Amended) The method of claim 1, wherein the active substance(s) is (are) selected from the following active substances:
 - peptide and non-peptide inhibitors of the cellular caspase-3, comprising
 - ♦ Z-DEVD-FMK
 - ♦ Ac-DEVD-CHO
 - ♦ Ac-DMQD-CHO
 - ♦ Z-D(OMe)E(OMe)VD(OMe)-FMK
 - ♦ Z-D(OMe)QMD(OMe)-FMK,
 - inhibitors of cellular caspases, which can activate caspase-3, comprising
 - ♦ peptide and non-peptide inhibitors of the caspase-9, comprising
 - o Z-LE(OMe)HD(OMe)-FMK
 - o Z-IETD-FMK
 - o Ac-LEHD-CHO
 - ♦ peptide and non-peptide inhibitors of the caspase-8, comprising
 - o Z-LE(OMe)TD(OMe)-FMK
 - o Ac-ESMD-CHO
 - o Ac-IETD-CHO (Alexis-Biochemicals)
 - o Z-IETD-FMK
 - ♦ peptide and non-peptide inhibitors of the caspase-10, comprising

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- o Ac-AEVD-CHO

- o Z-AEVD-FMK,

- peptide and non-peptide inhibitors of other caspases or granzyme B and pan-

- caspase inhibitors, comprising

- o Z-VAD-FMK

- o Z-VAD-(OMe)-FMK

- o Ac-YVAD-CHO

- o Z-YVAD-FMK

- o Z-VDVAD-FMK

- o Ac-LEVD-CHO,

- an inhibitory peptide, comprising Z-VAD-FMK or Z-DEVD-FMK,

- a non-peptide inhibitor of caspases,

- dominant-negative mutant of a caspase,

- an antisense-oligonucleotide, which specifically accumulates at the DNA sequence or m-RNA sequence coding for a cellular caspase and inhibits the transcription or translation thereof,

- a protein, which inhibitingly acts on caspases, comprising the cellular inhibitors of apoptosis proteins cIAP1, cIAP2, the X-linked inhibitor of apoptosis protein XIAP, the antiapoptotic protein Bcl-2 or the baculoviral protein p35,

- dsRNA oligonucleotides, which are suitable for the specific degradation of the mRNA's of a cellular caspase by the RNAi technology,

- an antibody or antibody fragment specific for a caspase or a fusion protein containing at least one antibody fragment, comprising a Fv fragment, which inhibits the protease activity of a caspase.

4. (Previously Presented) The method of claim 1, wherein the viral disease is caused by RNA or DNA viruses, comprising influenza viruses.

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5. (Previously Presented) A combination preparation for the prophylaxis or therapy of at least one viral disease, comprising at least two antiviral active substances, wherein at least one antiviral active substance is selected from the active substances according to claim 3, wherein the combination preparation can be used in the form of a mixture or as individual components for using them simultaneously or at different times at identical or different places.

6. (Previously Presented) A combination preparation for the prophylaxis or therapy of a viral disease, comprising at least one active substance according to claim 1 and at least one antivirally acting substance, which is a kinase inhibitor.

7. (Previously Presented) A combination preparation for the prophylaxis or therapy of a viral disease, comprising at least one active substance according to claim 1 and at least one antivirally acting substance, which is a 1-adamantanamine, a rimantadine, a neuraminidase inhibitor or a nucleoside analog comprising ribavirin.

8. (Previously Presented) The combination preparation according to claim 5 for the prophylaxis or therapy of an infection with negative-strand RNA viruses, comprising influenza viruses or Borna viruses.

9. (Previously Presented) A test system for finding active substances, which act on at least one cellular caspase, comprising caspase-3, such that a virus multiplication is inhibited, comprising:

a) at least one cell infectable with at least one virus and comprising at least one cellular caspase and at least one virus infecting the cells, or

b) at least one cell infectable with at least one virus and comprising at least one cellular caspase.

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10. (Previously Presented) The test system according to claim 9, wherein the virus is an RNA or DNA virus, comprising an influenza virus.

11. (Previously Presented) The test system according to claim 9 wherein the cell comprises at least one overexpressed caspase, comprising caspase-3.

12. (Previously Presented) The test system according to claim 9, comprises a cell, in which at least one gene coding for at least one dominant-negative mutant of at least one caspase is expressed.

13. (Previously Presented) A test system according to claim 9, further comprising a cell in which the expression for at least one caspase, comprising caspase-3, is inhibited.

14. (Previously Presented) A method for identifying at least one active substance for the prophylaxis or therapy of viral diseases, which substantially inhibits or inhibit the multiplication of viruses during viral diseases, comprising the following steps:

- a) bringing at least one test system according to claim 9 into contact with at least one potential active substance, and
- b) determining the effects on virus multiplication.

15. (Previously Presented) A method for preparing a drug for the prophylaxis or therapy of a viral disease, which substantially inhibits the multiplication of viruses during viral diseases, comprising the following steps:

- a) performing a test system according to claim 9, and
- b) reacting the active substance(s) with at least one auxiliary and/or additional substance.

16. (Previously Presented) A method for the prophylaxis or therapy of a viral infection, comprising an infection with an RNA negative-strand virus, comprising an

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influenza infection, comprising administering a physiologically effective dose of a pharmaceutical composition, comprising at least one caspase inhibitor, comprising a caspase-3 inhibitor.

17. (Previously Presented) The method according to claim 16, wherein the pharmaceutical composition further comprises at least one additional antiviral active substance, which is not a caspase inhibitor, comprising an inhibitor of one or several cellular kinases.

18. (Previously Presented) A combination preparation for the treatment of a viral infection, comprising at least one caspase inhibitor and another antiviral active substance, which is not a caspase inhibitor, comprising an inhibitor of one or several cellular kinases, each in a physiologically well tolerated dose, and galenic auxiliary and carrier substances, wherein the caspase inhibitor and the further antiviral active substance exist in a mixture or in separate galenic preparations, intended for simultaneous or successive administration.

19. (Previously Presented) The combination preparation according to claim 18, wherein the caspase inhibitor is selected from the group consisting of the substances according to claim 3 and mixtures of such substances.

20. (Currently Amended and Withdrawn) ~~The use of~~ A method of use of a combination preparation according to claim 18, wherein the further antiviral active substance is selected from the group consisting of neuraminidase inhibitors, nucleoside analogs, 1-adamantanamine, rimantadine, ribavirin, Relenza, 3-deazaadenosine, MEK inhibitors, comprising butadiene derivatives, flavon derivatives and benzamide derivatives, 2-(2-amino-3-methoxyphenyl)-4-oxo-4H-(1)benzopyran, U0126, PD18453, PD98059, inhibitors of a kinase of the NF-kB signal transduction pathway, comprising non-steroidal anti-inflammatory substances inhibiting the NF-kB activity, comprising phenyl alkyl acid derivatives comprising sulindac or derivatives of sulindac comprising

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sulindac sulfoxide, sulindac sulphone, sulindac sulphide, benzylamide sulindac analogs, salicylic acid derivatives, comprising salicylic acid or acetylsalicyl acid, salicylamide, salacetamide, ethebamide, diflunisal, olsalazine or salazosulphapyridine, curcumin, antioxidants comprising pyrrolidine dithiocarbamate (PDTC), oxicams, comprising piroxicam, vitamin E and derivatives thereof, comprising pentamethyl-hydroxychromane (PMC), 17 beta-oestradiol and derivatives thereof, polyphenols of the tea comprising Epigallocatechin-3-gallate (EGCG), Bayl 1-7182, peptides, which inhibit the interaction of at least two components of the NF-kB signal transduction pathway, comprising peptides binding to NEMO, proteasome inhibitors, comprising PS-341 and lactacystin, antisense-oligonucleotides, which specifically accumulate at the DNA sequence or mRNA sequence coding for a component of the NF-kB signal transduction pathway and inhibit the transcription or translation thereof, comprising antisense-nucleotide sequences specific for p65 or p50, dominant-negative mutants of a component of the NF-kB signal transduction pathway, dsoligonucleotides, which are suitable for the specific degradation of the mRNA's of a component of the NF-kB signal transduction pathway by the RNAi technology, antibodies and antibody fragments specific for a component of the NF-kB signal transduction pathway, or fusion proteins containing at least one antibody fragment, comprising a Fv fragment, which inhibit at least one component of the NF-kB signal transduction pathway, kinase-inhibiting flavon derivative or benzopyran derivative; kinase-inhibiting derivative of the 4H-1-benzopyran; flavopiridol derivative; 2-(2-amino-3-methoxyphenyl)-4-oxo-4H-(1)benzopyran; 7,12-dihydro-indolo (3,2-d)(1)benzazepin-6(5H)-on; 70H-staurosporine or a phosphokinase-inhibiting derivative of the 70H-staurosporine; butyrolactone; roscovitine; purvalanol A; emodin; anilinoquinazoline; phenylaminopyrimidine; triolimidazole; paullone; [4-(4-fluorophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)H-imidazole; 1,4-diamino-2,3-dicyano-1,4-bis(2aminophenylthio) butadiene; kinase-inhibiting derivative of the butadiene; [2-2'-amino-3'-methoxyphenyl)-oxa-naphthalen-4-on); [2-(2-chloro-4-iodo-phenylamino)-N-cyclo-propylmethoxy-3,4-difluoro benzamide; CEP-1347 (K17515) bis-ethylthiomethyl; tetrapyrrolic macrocycles; pyrimidone derivative; 3-aminomethylen-indoline derivative; pyrazolo (3,4-b) pyridine derivative; pyrazole derivative; 1,4-substituted piperidine

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derivative; lipoidic ammonium salt; dominant-negative mutant of a kinase of a cellular signal transduction pathway; antisense-oligonucleotide, which specifically accumulates at the DNA sequence or mRNA sequence coding for a kinase of a cellular signal transduction pathway and inhibits the transcription or translation thereof; dsoligonucleotides, which are suitable for degradation of the mRNA's from kinases of a cellular signal transduction pathway by the RNAi technology; antibodies and antibody fragments specific for a kinase or a fusion protein containing at least one antibody fragment, comprising a Fv fragment, which inhibits the kinase activity of a kinase module; or a peptide, which inhibits the interaction of at least two kinases activatable immediately after one another of a cellular signal transduction pathway, and mixtures of such substances.

21. (Previously Presented) A method for screening for prospective antiviral active substances, comprising the following steps:

- a) a cell containing a caspase, comprising caspase-3, is infected with a virus, comprising an RNA negative-strand virus, comprising an influenza virus,
- b) the cell is contacted with one or several prospective active substances,
- c) viral replication in the cell is determined,
- d) an active substance or a mixture of active substances is selected, if the viral replication measured in step c) is smaller than when executing steps a) to c) without a prospective active substance or with an inactive active substance,
- e) a selected active substance is contacted with a cell infected with a virus, which does not express or contain a caspase, in particular caspase-3, and the viral replication is measured, and the active substance is further selected, if the measurement of the viral replication does not result in a significant modification relative to a measurement when contacting said infected cell with an inactive active substance or without any active substance,

wherein the steps a) and b) may occur in any order or simultaneously, and wherein the steps a) to d) on the one hand and the step e) on the other hand may occur in any order or simultaneously.